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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/760,274	01/12/2001	John Sinden	GJE-21D2	3086

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EXAMINER

WILSON, MICHAEL C

ART UNIT	PAPER NUMBER
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1632

DATE MAILED: 12/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action

Application No.

09/760,274

Applicant(s)

SINDEN ET AL.

Examiner

Michael C. Wilson

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--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 25 October 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

- a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
- ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on 25 October 2004. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ they raise the issue of new matter (see Note below);
- (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____

3. ☒ Applicant's reply has overcome the following rejection(s): the double patenting rejection.
4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: see attached.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☐ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____

Claim(s) objected to: _____

Claim(s) rejected: 57, 58, 60-62, 64 and 76-86.

Claim(s) withdrawn from consideration: _____

8. ☐ The drawing correction filed on _____ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
10. ☐ Other: _____

MICHAEL WILSON
PRIMARY EXAMINER



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DETAILED ACTION

Applicant's arguments filed 10-25-04 have been considered in part. The new matter arguments could have been made when the amendment was filed.

Claims 1-48, 59 and 68-75 have been canceled. Claims 57, 58, 60-62, 64 and 76-86 remain pending and under consideration in the instant office action.

Claim Rejections - 35 USC § 112

Written Description

Claims 57, 58, 60-62, 64 and 76-86 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons of record.

Applicants cite Kawaguchi (Molecular and Cellular Neuroscience, 2001, 17:259-273) and Sakakibara (PNAS, 2002, 99(23)15194-1519). Sakakibara teaches musashi is a protein expressed in neural precursor cells including CNS stem cells. Kawaguchi teaches nestin is expressed in neural precursor cells. Applicants argue the human nestin-positive, musashi-positive pluripotent neural stem cells in the Declaration by Dr. Sinden were merely further characterized as expressing musashi 1, in addition to nestin. Applicants conclude the experimental results in the Declaration by Dr. Sinden should not be disqualified as evidence of written description. Applicants' arguments are not persuasive. The art does not teach nestin and musashi were expressed in the

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same populations of pluripotent neural stem cells. Sakakibara taught musashi was specific for the development of aqueductal ependymal cells and that musashi expression was highly restricted to cell populations in the ependyma lining the aqueduct. (pg 15198, col. 2, Discussion). Kawaguchi simply taught nestin was generic to neural precursor cells. The nestin-positive, musashi-positive, human, pluripotent, neural precursor cells described in the Declaration by Dr. Sinden as having the desired function *in vivo* have a narrower scope than nestin-positive, human, pluripotent, neural precursor cells described in the specification as originally filed. As such, applicants did not adequately describe that which was essential to obtain human neural precursor cells having the desired function, i.e. nestin-positive neural precursor cells expressing musashi. The experimental results in the Declaration by Dr. Sinden remain unpersuasive because the cells used in the experiment were of a narrower scope than those described in the specification as originally filed and because musashi expression may be essential to obtain nestin-positive neural precursor cells with the desired function in humans.

Please argue written description and enablement rejections separately.

Please include a separate heading for the written description arguments.

New Matter

The phrase "a disorder associated with damage to, or loss of, brain cells in a mammal" in claims 57, 81 and 85 remains new matter.

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The phrase "wherein said cells are immortal prior to said transplanting and differentiate after said transplanting" in claim 57 is new matter.

The phrase "wherein said transplanting improves brain function of said mammal" in claims 57 and 81 is new matter.

The phrase "a disorder associated with damage to, or loss of, brain cells in the hippocampus of said mammal" in claim 58 is new matter.

The phrase "wherein said transplanting improves cognitive function of said mammal" in claims 57 and 81 is new matter.

Treating humans as in claims 82 and 86 is new matter.

The specification as a whole does not support using any nestin-positive, neuroepithelial cells as newly amended because the specification only taught using hippocampal neuroepithelial cells.

The specification does not support improving any "brain function" as newly amended by adding neuroepithelial cells because the specification only taught using a model of cognitive function (pg 10).

The new matter arguments have been considered but will not be addressed after final because of the extensive time required doing so. The new matter arguments should be repeated upon filing an RCE and will be addressed in detail at that time.

Please include a separate heading for the new matter arguments.

Enablement

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Claims 57, 58, 60-62 and 76-86 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a cognitive deficit in a rat caused by a hippocampal lesion comprising administering mouse, hippocampal, nestin-positive, pluripotent, neuroepithelial cells comprising a vector encoding tsA58 operably linked to the H-2Kb promoter to the hippocampus of the rat such that the cognitive deficit is treated, does not reasonably provide enablement for i) using any pluripotent, nestin-positive neuroepithelial cells to treat any disorder associated with damage to, or loss of, any brain cells, ii) treating damaged brain cells by implanting genetically modified cells anywhere within the brain, iii) using nestin-positive, pluripotent, neuroepithelial cells to treat a disorder associated with damage to, or loss of, brain cells in a human, or iv) using any "conditionally immortal" cells as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims for reasons of record.

Applicants cite Kawaguchi (Molecular and Cellular Neuroscience, 2001, 17:259-273) and Sakakibara (PNAS, 2002, 99(23)15194-1519). Sakakibara teaches musashi is a protein expressed in neural precursor cells including CNS stem cells. Kawaguchi teaches nestin is expressed in neural precursor cells. Applicants argue the human nestin-positive, musashi-positive pluripotent neural stem cells in the Declaration by Dr. Sinden were merely further characterized as expressing musashi 1, in addition to nestin. Applicants conclude the experimental results in the Declaration by Dr. Sinden should not be disqualified as evidence of enablement. Applicants' arguments are not

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persuasive. The art does not teach nestin and musashi were expressed in the same populations of pluripotent neural stem cells. Sakakibara taught musashi was specific for the development of aqueductal ependymal cells and that musashi expression was highly restricted to cell populations in the ependyma lining the aqueduct. (pg 15198, col. 2, Discussion). Kawaguchi simply taught nestin was generic to neural precursor cells. The nestin-positive, musashi-positive, human, pluripotent, neural precursor cells described in the Declaration by Dr. Sinden as having the desired function *in vivo* have a narrower scope than nestin-positive, human, pluripotent, neural precursor cells described in the specification as originally filed. As such, applicants did not adequately teach those of skill that which was essential to obtain human neural precursor cells having the desired function, i.e. musashi expression. The experimental results in the Declaration by Dr. Sinden remain unpersuasive because the cells used in the experiment were of a narrower scope than those described in the specification as originally filed and because musashi expression may be essential to obtain nestin-positive neural precursor cells with the desired function in humans.

Double Patenting

The rejection of claims 57, 58, 60-62 and 76-86 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of copending Application Nos. 10/342692 and 10/376119 has been withdrawn in view of the terminal disclaimers filed 10-25-04.

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Conclusion

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on 571-272-0804.

The official fax number for this Group is (703) 872-9306.
Michael C. Wilson



MICHAEL WILSON
PRIMARY EXAMINER